Selección de Resúmenes de Menopausia

Semana del 17 al 23 de marzo 2021

María Soledad Vallejo. Clínica Quilín. Universidad de Chile

Eur J Cancer. 2021 Mar 16;148:95-102.doi: 10.1016/j.ejca.2021.02.007. Online ahead of print.

Riesgo de cáncer de mama y terapia de reemplazo hormonal, entre portadoras de BRCA después de una salpingo-ooforectomía de reducción de riesgo

Breast cancer risk and hormone replacement therapy among BRCA carriers after risk-reducing salpingo-oophorectomy

Rachel Michaelson-Cohen 1 , Shira Gabizon-Peretz 2 , Shunit Armon 3 , Naama Srebnik-Moshe 4 ,

Introduction: BRCA1/BRCA2 mutation carriers often undergo risk-reducing salpingo-oophorectomy (RRSO) before natural menopause, raising the issue of hormonal replacement treatment (HRT) use. There is conflicting evidence on the effect of HRT on breast cancer (BC) risk, and there are limited data on risk based on age at exposure. In the general population, HRT users have an increased BC risk (hazard ratio = 1.34). We assessed the impact of short-term HRT use on BC risk among healthy BRCA1/2 mutation carriers, with emphasis on age at exposure to HRT. Methods: A retrospective cohort of 306 consecutive healthy BRCA1/2 mutation carriers who had undergone RRSO was followed up for a mean of 7.26 years. We compared BC incidence over time in carriers who received HRT with that in those who did not receive. Results: Thirty-six of the carriers were diagnosed with BC, 20 of 148 patients (13.5%) in the HRT group compared with 16 of 155 (10.3%) in the non-HRT group (odds ratio [OR] = 1.4, 95% confidence interval [CI] = 0.7-2.7). In women who were aged 45 years or younger at RRSO, HRT did not affect BC rates. However, in those older than 45 years at RRSO, BC rates were significantly higher in HRT users than in non-users (OR = 3.43, $p < 0.05$, 95% CI = 1.2-9.8). Conclusions: In BRCA1/BRCA2 carriers in this study, short-term post-RRSO HRT use was associated with a threefold risk of BC in carriers older than 45 years. These results suggest that risk may be related to time of exposure to HRT around the natural age of menopause, even among BRCA1/2 carriers. Further studies are needed for validation and to guide future recommendations.

Clin Breast Cancer. 2021 Feb 17;S1526-8209(21)00047-1.doi: 10.1016/j.clbc.2021.02.005. Online ahead of print.

Uso de aspirina y riesgo de cáncer de mama: Un meta-análisis de estudios observacionales de 1989 a 2019

Aspirin Use and Risk of Breast Cancer: A Meta-analysis of Observational Studies from 1989 to 2019

Shaodi Ma, Cijuan Guo, Chenyu Sun, Tiantian Han, Huimei Zhang, Guangbo Q, Yuemeng Jiang, Qin Zhou, et al.

Background: Some evidence shows that aspirin can reduce the morbidity and mortality of different cancers, including breast cancer. Aspirin has become a new focus of cancer prevention and treatment research at present, however, clinical studies found conflicting conclusions of its anticancer characteristics. Materials and methods: A systematic literature search was performed in 8 electronic databases. The pooled relative risk (RR) with 95% confidence interval (CI) was calculated using the random effects model to estimate the effect of aspirin on breast cancer. Results: Forty-two published articles with 99,769 patients were identified. The meta-analysis showed a significant decrease in breast cancer risk with aspirin use (RR, 0.92; 95% CI, 0.89-0.96; I2 = 72%). Aspirin use decreased the risk of hormone receptor-positive tumors (estrogen receptor [ER]-positive RR, 0.89; 95% CI, 0.82-0.97; I2=54%; progesterone receptor [PR]-positive RR, 0.86; 95% CI, 0.78-0.95; I2=32%; ER- and PR-positive RR, 0.92; 95% CI, 0.85-1.00; I2=45%) and reduced the risk of breast cancer in postmenopausal women (RR, 0.92; 95% CI, 0.86-0.98; I2=59%). Further analysis showed that for the in situ breast cancer, regular-dose and more than 3 years use of aspirin were associated with the reduced risk of breast cancer. Conclusion: This meta-analysis suggested that aspirin may reduce the overall risk of breast cancer, reduce the risk of breast cancer in postmenopausal women, hormone receptor-positive tumors, and in situ breast cancer. Larger, multicenter clinical studies are needed to find the optimal dose range, frequency, and duration of the aspirin use to explore the best benefit-risk ratio.

Menopause. 2021 Mar 15. doi: 10.1097/GME.0000000000001766. Online ahead of print.

Estudio prospectivo controlado sobre la función sexual y angustia de la mujer, relacionada con el sexo, hasta 12 meses después de la salpingo-ooforectomía bilateral premenopáusica de reducción de riesgo

A prospective controlled study of sexual function and sexually related personal distress up to 12 months after premenopausal risk-reducing bilateral salpingo-oophorectomy

Rakibul M Islam 1 , Susan R Davis, Robin J Bell, Trevor Tejada-Berges, Caspar David Wrede, et al.

Objective: Premenopausal risk-reducing bilateral salpingo-oophorectomy (RRBSO) may impair sexual function, but the nature and degree of impairment and impact of estrogen therapy on sexual function and sexually related personal distress after RRBSO are uncertain. Methods: Prospective observational study of 73 premenopausal women at elevated risk of ovarian cancer planning RRBSO and 68 premenopausal controls at population risk of ovarian cancer. Participants completed the Female Sexual Function Index and the Female Sexual Distress Scale-Revised. Change from baseline in sexual function following RRBSO was compared with controls at 12 months according to estrogen therapy use. Results: Baseline sexual function domains did not differ between controls and those who underwent RRBSO and subsequently initiated (56.2%) or did not initiate (43.8%) estrogen therapy. At 12 months, sexual desire and satisfaction were unchanged in the RRBSO group compared with controls. After RRBSO, nonestrogen therapy users demonstrated significant impairment in sexual arousal (β-coefficient (95% confidence interval) -2.53 (-4.86 to -0.19), $P < 0.03$), lubrication (-3.40 (-5.84 to -0.96), $P < 0.006$), orgasm (-1.64 (-3.23 to -0.06), $P < 0.04$), and pain (-2.70 (-4.59 to 0.82), $P < 0.005$) compared with controls. Although sexually related personal distress may have been more likely after RRBSO, irrespective of estrogen therapy use, there was insufficient data to formally test this effect. Conclusions: The findings suggest premenopausal RRBSO adversely affects several aspects of sexual function which may be mitigated by the use of estrogen therapy. Further research is needed to understand the effects of RRBSO on sexual function and sexually related personal distress, and the potential for estrogen therapy to mitigate against any adverse effects.

Int J Epidemiol. 2021 Jan 17;dyaa284.doi: 10.1093/ije/dyaa284. Online ahead of print.

Estradiol y riesgo de infarto al miocardio en mujeres: estudio de cohorte con participantes del Biobanco del Reino Unido

Oestradiol and the risk of myocardial infarction in women: a cohort study of UK Biobank participants

Sanne A E Peters 1 2 3 , Mark Woodward 1 3 4

Background: It is commonly assumed that high oestradiol levels in women are cardioprotective. We assessed the association between oestradiol and the risk of incident myocardial infarction (MI) in women. Methods: We used data from 263 295 female UK Biobank participants [mean age 56.2; standard deviation (SD) 8.0 years] without previous cardiovascular disease (CVD). Associations of oestradiol with age and other cardiovascular risk factors were assessed. Cox proportional hazards models estimated crude, ag- and multiple-adjusted hazard ratios (HR) for MI associated with oestradiol levels. Results: After a mean follow-up of 9 years, 2206 incident cases of MI had been recorded, including 230 events among the 57 204 women (mean age 48) with detectable oestradiol levels. In the unadjusted analyses, a unit higher in log-transformed oestradiol was associated with an HR [95% confidence interval (CI) for MI of 0.73 (0.58; 0.92)]. After adjusting for age, this HR became 0.94 (0.75; 1.17), and after further adjusting for classical CVD risk factors, it was 1.05 (0.83; 1.31. Results were similar in subgroup analyses defined by age, menopausal status, socioeconomic status, contraceptive pill use and the use of hormone replacement therapy. The multivariable-adjusted HR for the 171 431 women (mean age 59) with undetectable levels of oestradiol, compared with those with detectable levels, was 0.97 (0.92; 1.02). Conclusions: Higher levels of oestradiol were not associated with a decreased risk of MI. The presumed cardioprotective effects of oestradiol seem to be largely confounded by age and further confounded by other cardiovascular risk factors.

Int J Cancer. 2021 Mar 17.doi: 10.1002/ijc.33563. Online ahead of print.

Tasa de cáncer de mama después de la ooforectomía: Un estudio de cohorte prospectivo de Dinamarca

Breast Cancer Rate after Oophorectomy: A Prospective Danish Cohort Study

Trine Koch 1 2 , Jeanette Therming Jørgensen 3 , Jane Christensen 4 , Christian Dehlendorff 4 , et el.

The association between oophorectomy and risk of breast cancer in the general population is uncertain. The aim of this study was to determine the breast cancer rate in women from the general population after oophorectomy (performed before/after menopause), and whether this varies by use of hormone replacement therapy (HRT), hysterectomy, body mass index (BMI) and shift work. The study included 24,409 female nurses (aged ≥45 years) participating in the Danish Nurse Cohort. Nurses were followed from cohort entry until date of breast cancer, death, disappearance, emigration or end of follow-up at 31st December 2018, whichever came first. Poisson regression with log-transformed person-years as the offset examined the association between oophorectomy and breast cancer (all ages and stratified by menopausal status at time of oophorectomy). The potential modifying effect of HRT use, hysterectomy, BMI and shift work on the associations was estimated. During 502,463 person-years of follow-up, 1,975 (8.1%) nurses were diagnosed with breast cancer. Bilateral oophorectomy was associated with reduced breast cancer rate compared to nurses with preserved ovaries, adjusted rate ratio (aRR) (95% confidence interval, CI): 0.79 (0.64; 0.99). Similar associations (magnitude and direction) were detected for unilateral oophorectomy and when stratifying according to menopausal status at time of oophorectomy, but without statistical significance. Unilateral and bilateral oophorectomy is associated with a reduced breast cancer rate in women from the general population. This association is not modified by use of HRT, hysterectomy, BMI or shift-work.

Maturitas. 2021 Apr;146:1-8.doi: 10.1016/j.maturitas.2020.12.010. Epub 2021 Jan 8.

Tiempo, dosis y adherencia a la TRH y riesgo de fractura en mujeres con síndrome menopáusico en Taiwán: estudio anidado de caso-control

Timing and dosage of and adherence to hormone replacement therapy and fracture risk in women with menopausal syndrome in Taiwan: A nested case-control study

Cherry Yin-Yi Chang 1 , Fuu-Jen Tsai 2 , Jian-Shiun Chiou 3 , Mu-Lin Chiu 4 , Ting-Hsu Lin 5 , et el.

Objective: To investigate the association between hormone replacement therapy (HRT) and the risk of bone fracture in menopausal women in Taiwan. Study design: The longitudinal, population-based, nested case-control study in Taiwan involved 5269 women aged > 45 years with fractures and 21,076 matched randomly selected controls without fractures. A conditional logistic regression model of analysis was employed. Main outcome measures: The association between the risk of bone fracture and various HRT-related parameters, including the timing, dosage, and adherence, was investigated. Results: Women with menopausal syndrome were protected from fractures when they received hormone drugs at high cumulative defined daily doses (DDDs) (Cumulative DDDs≥360) (odds ratio [OR]: 0.90, 95 % confidence interval [CI]: 0.82-0.99) and when their adherence was high (over 0.5) (OR: 0.70, 95 % CI: 0.60-0.82). The risk of fracture also decreased with high cumulative DDDs and high adherence combined (OR: 0.71, 95 % CI: 058-0.86). Subgroup analyses suggested that estrogen-containing regimens showed a protective effect against fractures at high cumulative DDDs or when adherence was high. Similar results were also observed with progestogen-containing regimens. Past exposure to an estrogen-containing regimen showed a protective effect against fractures when adherence was high. Past exposure to a progestogen-containing regimen showed a protective effect against fractures at high cumulative DDDs and when adherence was high. Conclusions: The results indicate that past exposure to estrogen-containing or progestogen-containing regimens exerts protective effects against bone fracture. These effects increased with higher cumulative DDDs and with adherence in a dose-dependent manner.

Climacteric. 2021 Mar 15;1-12.doi: 10.1080/13697137.2021.1892627. Online ahead of print.

Menopausia y quejas cognitivas: ¿están las hormonas ováricas relacionadas con el deterioro cognitivo subjetivo?

Menopause and cognitive complaints: are ovarian hormones linked with subjective cognitive decline?

R Reuben 1 , L Karkaby 1 2 , C McNamee 1 , N A Phillips 3 , G Einstein 1 2 4 5

Subjective cognitive decline (SCD) and the loss of ovarian hormones after menopause have been independently linked to later-life Alzheimer's disease (AD). The objective of this review was to determine whether menopause and the loss of ovarian hormones contribute to cognitive complaints and SCD in women. This would suggest that SCD at the menopausal transition might be an important marker of eventual cognitive decline and AD. We conducted a literature search using PubMed, PsycINFO and Web of Science in July 2020. All English-language studies assessing SCD and cognitive complaints with respect to menopause and ovarian hormones were included. A total of 19 studies were included. Studies found that cognitive complaints increased across the menopause transition and were associated with reductions in attention, verbal and working memory, and medial temporal lobe volume. Women taking estrogen-decreasing treatments also had increased cognitive complaints and reduced working memory and executive function. The current literature provides impetus for further research on whether menopause and the loss of ovarian hormones are associated with cognitive complaints and SCD. Clinicians may take particular note of cognitive complaints after menopause or ovarian hormone loss, as they might presage future cognitive decline.

J Am Heart Assoc. 2021 Mar 15;e019310.doi: 10.1161/JAHA.120.019310. Online ahead of print.

El estrógeno desempeña un papel crucial en la autofagia mitocondrial dependiente de Rab9, retrasando la senescencia arterial

Estrogen Plays a Crucial Role in Rab9-Dependent Mitochondrial Autophagy, Delaying Arterial Senescence

Yuichi Sasaki 1 , Yoshiyuki Ikeda 1 , Yoshihiro Uchikado 1 , Yuichi Akasaki 1 , Junichi Sadoshima 2 , et el.

Background The risk of cardiovascular disease is known to increase after menopause. Mitochondria, which undergo quality control via mitochondrial autophagy, play a crucial role in the regulation of cellular senescence. The aim of this study was to investigate whether the effect of estrogen-mediated protection from senescence on arteries is attributed to the induction of mitochondrial autophagy. Methods and Results We used human umbilical vein cells, vascular smooth muscle cells, and 12-week-old female C57BL/6 mice. The administration of 17β-estradiol (E2) to cells inhibited cellular senescence and mitochondrial dysfunction. Furthermore, E2 increased mitochondrial autophagy, maintaining mitochondrial function, and retarding cellular senescence. Of note, E2 did not modulate LC3 (light chain 3), and ATG7 (autophagy related 7) deficiency did not suppress mitochondrial autophagy in E2-treated cells. Conversely, E2 increased the colocalization of Rab9 with LAMP2 (lysosomal-associated membrane protein 2) signals. The E2-mediated effects on mitochondrial autophagy were abolished by the knockdown of either Ulk1 or Rab9. These results suggest that E2-mediated mitochondrial autophagy is associated with Rab9-dependent alternative autophagy. E2 upregulated SIRT1 (sirtuin 1) and activated LKB1 (liver kinase B1), AMPK (adenosine monophosphate-activated protein kinase), and Ulk1, indicating that the effect of E2 on the induction of Rab9-dependent alternative autophagy is mediated by the SIRT1/LKB1/AMPK/Ulk1 pathway. Compared with the sham-operated mice, ovariectomized mice showed reduced mitochondrial autophagy and accelerated mitochondrial dysfunction and arterial senescence; these detrimental alterations were successfully rescued by the administration of E2. Conclusions We showed that E2-induced mitochondrial autophagy plays a crucial role in the delay of vascular senescence. The Rab9-dependent alternative autophagy is behind E2-induced mitochondrial autophagy.